combined treatment are characterized by the significant cubic trend ($P = 0.00284$ and $P = 0.029$, respectively). Changes of miRNA-126 expression level during post-treatment follow-up were not characterized by the definite trend and not correlated with changes of other miRNAs expression level. It was shown the significant correlation between miRNA-25 and miRNA-205 expression levels, but was not found the trend of these miRNAs level changes.

Conclusion: The clinical utility of the circulating miR-19b and miR-125b expression analysis from this study remains to be validated in large cohorts of patients with different histological types of tumors, at the different stage of disease and outcomes. One of the criteria for inclusion in the group must be susceptibility and/or resistance to therapy.

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Tumour secreted factors cathepsins D and L induce pro-angiogenic changes in human omental microvascular endothelial cells (HOMECs) in ovarian cancer metastasis

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Background: Epithelial ovarian cancer frequently metastasizes to the omentum, a process that requires pro-angiogenic activation of HOMECs by tumour -secreted factors in their microenvironment. We have previously shown that ovarian cancer cells secrete a range of factors with possible roles in metastatic angiogenesis including the lysosomal proteases cathepsin D (CD) and cathepsin L (CL). However, the role of these proteases in ovarian cancer metastasis to the omentum is not fully understood.

Aim: To investigate whether proliferative effects of CD and CL are dependent on their catalytic activity in HOMECs.

To investigate the intracellular signalling kinases activated by CD and CL.

Method: HOMEC proliferation was assessed by using a colorimetric (WST1) assay. Potential signalling pathways were examined by phosphokinase array and ELISAs. pH experiments were carried out examine whether the observed effects were due to the catalytic activity of CD and CL.

Result: CD and CL (50 ng/ml) significantly increased HOMEC proliferation to 141 ± 27% ($p = 0.001$, $n = 50$) and 151% ± 34% ($p = 0.001$, $n = 45$) respectively vs. control (100%) 72 h post-treatment. Inhibitors of CD and CL enzyme activity had no effect on HOMEC proliferation and subsequent pH data suggest a non-proteolytic mitogenic activity of these cathepsins. Both proteins induced phosphorylation of ERK1/2, AKT and p38α to ~2, ~1.5 and ~1.5 folds respectively relative to total levels (compared to control).

Conclusion: CD and CL induced proliferation in HOMECs. CD and CL may non- proteolytically contribute to pro-angiogenic responses of the omental microvasculature. Induction of phosphorylation of proliferative kinases ERK1/2, AKT and p38α suggest possible downstream signalling cascades of these proteins.

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Expression analysis 20 miRNAs in the clear cell renal cell carcinomas and surrounding tissues

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RCC is one of the main problems in oncourology. MiRNA expression profiles are highly specific for malignant tumors of different locations, and can be used to detect pathological molecular biomarkers and to develop the optimal treatment for each patient. Selection of miRNAs associated with the formation and development of malignant tumors in the kidney was performed using computer databases miRWalk (http://www.ma.uni-hei-delberg.de/apps/zmf/mirwalk/) and miRBase (http://www.mir-base.org/). Paired samples of tumor and histologically normal tissue from 46 patients with RCC were studied. RNA was isolated by phenol–chloroform extraction and treated with RNase-free DNase after isolation. MiRNA expression analysis was performed by RT-qPCR using Applied Biosystems (USA) kits: TaqMan® MicroRNA Assays, TaqMan® MicroRNA Reverse Transcription Kit, TaqMan® Fast Universal PCR Master Mix (2x). RNU6B was used as reference miRNA. Quantity alterations of 20 microRNAs (hsa-miR-219, -203, -148a, -129, -9, -34a, -34b, -34c-3p, -127, -193a-5p, -191, -17, -24 -2*, -339 -3p, -212, -375, -125b, -124a, -132, -137) were determined in samples of tumor compared to normal tissue biopsy from the kidney of each patient. It was shown that the expression of studied miRNAs usually decreased in RCC tumors. The largest decrease of expression was observed for miR-129, which expression was10–350-fold reduced in 93% of the samples ($P < 0.05$) with no change of expression in the remaining 7% of cases. MiR-375 (80% of cases,10–270-fold decrease), miR-34b (79% of cases, 10–60-fold decrease), miR-124a (70% of cases, 10–200-fold decrease) also frequently showed reduced expression in tumors. In addition to the aforementioned ones, it had been shown that expression in the tumor compared with histologically normal tissue from the same patient was significantly decreased in more than half of the cases for miR-125b, miR-127, miR-203, miR-34c-3p, miR-9. Despite the fact that in 50% of cases decreased expression of miR-9 was detected, it was the only of studied microRNA with a significant increase in the expression in 21% of cases in 10–160 times ($P < 0.05$). Associations between the expression of investigated miRNAs and gender and age were not noted. Dealing with each miRNA alone, we could not detect the dependence of expression alteration of 20 selected miRNAs from the stage or degree of tumor differentiation of the studied RCC samples. However, the analysis of the expression profile of